REMARKS/ARGUMENTS

Substitute Specification

Applicant provides a marked up copy of the specification as requested by the Examiner.

Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The Examiner contends that Claims 24-27 recite the limitation "the mechanical means" or "said mechanical means" without there being a sufficient antecedent basis for the same. The claims have been amended to overcome such concern. Applicant also amends Claim 27 to address other issues raised by the Examiner with respect to alleged indefiniteness with respect to the use of "length" in the claim. Claim 41 has also been amended to address the Examiner's concern relating to the intermittent motion of the catheter.

Rejection of Claims 20-30 Under 35 U.S.C. §102(e) as Anticipated by Cragg et al.

The Examiner contends that Claims 20 and 26 are anticipated by Cragg et al. because Cragg et al. disclose a device where a thrombolytic agent is pumped through a catheter and delivered using a power injector or programmable pump, allegedly thereby providing a "means for providing mechanical action" as claimed in the present invention. The Examiner also contends that Cragg et al. disclose that the catheter can be advanced back and forth by a physician, thereby providing mechanical action to the vessel. Applicant respectfully traverses the Examiner's rejection of claims for the reasons as set forth below.

At the outset, Applicant directs the Examiner's attention to the claims, as amended, which are believed to further distinguish the Cragg et al. reference. The device disclosed in the Cragg et al. patent utilizes "lysis jets" of the lytic agent to effect mechanical action on a clot. In contrast, the present invention uses motion of the catheter itself to effect mechanical action, whether the catheter itself is moved by action of a motor, or whether movement of the catheter is caused by the pulsing of lytic agent through the catheter itself. In some embodiments, the present invention also infuses lytic agent passively through a catheter to act chemically on a clot. Moreover, the Cragg et al. device is similar to many existing devices on the market that are utilized only during a particular procedure

for a short period of time, in contrast to the present invention which is designed for use over an extended period of time. Indeed, Cragg et al. discusses the partial removal of a clot during a short procedure, with the remaining clot necessitating treatment with long term infusion (see Col. 6 of Cragg et al. patent). Using the present invention, the "dual treatment" as described by Cragg et al. is eliminated through a single, more lengthy procedure whereby the catheter is mechanically moved to break up a clot, while passive infusion of a lytic agent is also provided over a several hour period of time. Cragg et al. teach away from utilizing their device for an extended several hour period of time. For example, Cragg et al. indicate their treatment time is only 5 minutes (Col. 6, lines 46-49). Because Cragg et al.'s device has no motor or motor controller, but instead, relies upon high pressure sprays of lytic agent, Cragg et al. is viewed as a teaching away from the present invention. Because the present invention is directed to the physical movement of the catheter itself, preferably such movement being over a long period of time, to physically break up clots. Moreover, the movement of the catheter by a physician as mentioned in Cragg et al. (Col. 3, lines 55-58) is solely to facilitate positioning of the side holes in the catheter to be adjacent to a clot, thereby permitting the lysis jets to be directed to the clot. Thus, as disclosed in Cragg et al., the movement by the physician of the catheter is incapable of providing any mechanical action to disrupt the clot itself, as is disclosed and claimed by the present invention.

Moreover, Cragg et al.'s device would be incapable of practical use in the method of the present invention given that Cragg et al. only teach the use of a power injector having a reservoir that contains only about 200 cc and the maximum programmable delay time on the injector is only 45 seconds. As such, Applicant calculates that the Cragg et al. device would need to be reloaded every 6.7 minutes, thus making the Cragg et al. device impracticable for utilization over a protracted period of time, which is one aspect of several embodiments of the present invention. Cragg et al. suggest 5 cc's a second, every ten seconds, which translates into over 43,000 cc's in a 24 hour period. It would therefore not be safe to operate the Cragg et al. device more than 10 - 15 minutes or else a patient would be subject to fluid volume overload.

For all the reasons as stated above, and in view of the claim amendments, Applicant respectfully requests that the Examiner reconsider and withdraw all §102 rejections of claims based upon the Cragg et al. reference.

Rejection of Claims Under 35 U.S.C. §103

The Examiner contends that Claims 41 and 42 are obvious in view of a combination of Cragg et al. in view of Monetti et al. Applicant incorporates by reference the arguments as set forth above with respect to the Cragg et al. reference. The Examiner admits that Cragg et al. fail to teach a programmable motor which regulates intermittent movement of a catheter. The Examiner contends, however, that Monetti et al. provide such a teaching and further, that it would have been obvious to one of ordinary skill in the art at the time of the present invention to combine the teachings of Monetti et al. with Cragg et al. to arrive at Applicant's invention. Applicant respectfully disagrees.

Monetti et al. discloses a hand-held, finger-operated drive motor which imparts a spinning action to a catheter. Applicant submits that it would not be obvious to one of ordinary skill in the art at the time of the present invention to combine the teachings of Cragg et al. with Monetti et al. Specifically, it would not be obvious to combine Cragg et al.'s teaching of a lytic jet with a hand-held, motor operated device to impart a spinning action to a catheter. Moreover, Monetti et al. do not teach or suggest the use of a programmable motor controller. It is not clear at all that the catheter of Cragg et al. could be modified to be controlled by the motor of Monetti et al. Moreover, given that Cragg et al. merely teach that a physician positions a catheter to be adjacent to a clot, rather than teaching mechanical action of the catheter to disturb the clot itself, is viewed as a teaching away from a combination of Cragg et al. with Monetti et al. Furthermore, neither reference teach or suggest the lengthy resident times of a moving catheter inside a patient - both teach away from such an application.

Applicant submits that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggesting supporting the combination. *ACS Hospital Systems v. Montofiore Hospital*, 221 USPQ 929, 933 (Fed.Cir. 1974). It appears that in the present case the only suggestion for the Examiner's combination of the

teachings in Cragg et al. improperly stems from the Applicant's own disclosure and not from the cited reference. At best, the Examiner's comments regarding obviousness appear to amount to an assertion that one of ordinary skill in the relevant art would have been able to arrive at Applicant's invention because they would have had the necessary skills to carry out the requisite process steps, provided that they possessed the unique device as set forth in the present claims. This is an inappropriate standard for obviousness. In brief, the Cragg et al. reference, alone or in combination with any other prior art, does not provide an impetus necessary to cause one skilled in the art to rely upon the Cragg et al. reference in the way the Examiner has done.

It is well established that an evaluation of the obviousness or non-obviousness of claims must not be made with the benefit of hindsight using the present application as a blueprint to reconstruct the claimed invention from the references. See *Interconnect Planning Corporation v. Feil*, 227 USPQ 543 (Fed.Cir. 1985). Applicant submits that the Examiner's examination of the present invention should not be predicated upon the obviousness of particular features but rather, should be based upon an evaluation of the invention as a whole. Again, given the lack of any suggestion or teaching in Cragg et al. to use a catheter which itself provides mechanical disruption of a thrombus, and which incorporates the use of features admittedly absent in Cragg et al. (e.g., the impossibility that use of the Cragg et al. device could accomplish the long term indwelling procedures contemplated by the present invention, etc.), leads to the conclusion that the Cragg et al. reference, alone or in combination, does not render the present invention obvious.

In arguing that it would have been obvious to make and use the claimed invention given the teachings of Cragg et al., the Examiner seems in essence to be stating that it would have been "obvious to try" modifying various parameters, and indeed selecting entirely different structures having distinct identifying features and capabilities, in order to produce the claimed invention. The Federal Circuit has provided clear direction with respect to arguments based on an "obvious to try" theory. The court has held that an "obvious to try" situation exists when a general disclosure may pique a scientists curiosity, such that further investigation might be done as the result of a disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued. *In re Eli Lilly & Co.*,

14 USPQ 2d 1741, 1743 (Fed.Cir. 1990). The court held, however, that "obvious to try" is not to be equated with obviousness under 35 U.S.C. §103. See *Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ 2d 1923, 1928 (Fed.Cir. 1990).

A rejection based on §103 clearly must rest on a factual basis, and these facts must be interpreted without hindsight reconstruction of the invention from the prior art. "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification." *In re Fritch*, 23 USPQ2d 1780, 1783-84 (Fed. Cir. 1992). Moreover, the motivating suggestion must be explicit. *Winner International Royalty Corporation v. Wang*, 48 USPQ2d 1139 (D.C, D.C. 1998) ("there must have been some explicit teaching or suggestion in the art to motivate one of even ordinary skill to combine such elements so as to create the same invention"). That individual elements of the inventions are old can be found in the prior art is irrelevant. *Grain Processing Corp. v. American Maize Products Co.*, 5 USPQ2d 1788 (Fed. Cir. 1988). The Examiner should not be able to pick and choose individual elements from multiple references to recreate the invention. *Polaroid Corp. v. Eastman Kodak Co.*, 229 USPQ 561 (Fed. Cir.), *cert. denied*, 479 U.S. 850 (1996). In determining the scope and content of the prior art, and determining whether the prior art suggested the claimed invention, the references "must be read as a whole and consideration must be given where the references diverge and teach away from the claimed invention". *Akzo N.V. v. United States Int'l Trade Commission*, 1 USPQ2d 1241 (Fed. Cir. 1986) *cert denied,* U.S. 909 (1987); *Panduit Corp. v. Dennison Mfg. Co.*, 1 USPQ2d 1593 (Fed. Cir), *cert denied*, 481 U.S. 1052 (1987).

"The best defense against the subtle, but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references." *In re Dembiczak*, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999). Moreover, particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected components for combination in the manner claimed. *In re Kotzab*, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). Here, there is no teaching or suggestion in any of the cited references to support a rejection under §103. For example, the physical motion of a catheter itself between its distal and proximal ends and that is sufficient to disturb a thrombus, is

not present in the cited prior art, nor are the long time periods; the slow rotational speeds; the programability of movement; etc. involved in the present method taught or suggested in the prior art. For the foregoing reasons, Applicant respectfully submits that neither Cragg et al. or Monetti et al. provide sufficient suggestions or teachings to direct one of ordinary skill in the art to make the present invention and as such, Applicant respectfully requests the Examiner to withdraw all §103 rejections predicated thereon. The Examiner's reconsideration of the present rejection and favorable review of the present claims is therefore appreciated.

Prior Art Made of Record, But Not Relied Upon

Applicant has had an opportunity to review the Shiber, Kotula et al. and Nita et al. references. Applicant does not believe that any of such references, alone or in combination with any other prior art references, would render any of the claimed inventions obvious.

Applicant's counsel respectfully requests the courtesy of a telephone interview in the event the Examiner has any further questions or concerns regarding any of pending claims. Applicant's counsel can be reached directly at (303) 863-2977.

Attached hereto is a marked up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version With Markings to Show Changes Made**."

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1-3, 9-14, 16, 20, 24-27, 31 and 41-42 have been amended as follows:

1. (Twice Amended) A thrombolytic device comprising:

a catheter having a catheter wall, a proximal end, a distal end, and at least one lumen;
a motor attached to said proximal end of said catheter for imparting motion to said catheter between said distal end and said proximal end, such motion causing physical movement of said catheter that is sufficient to disturb a thrombus[said catheter].

2. (Once Amended) A thrombolytic device as in claim 1, wherein:

said [mechanical element is chosen] motor comprising a device selected from the group consisting of a vibrational device, a rotational device, a bi-rotational device, an[d] expansile device, a wave-like undulating device, and a longitudinally-actuated device.

3. (Once Amended) A thrombolytic device as in claim 1, wherein said [mechanical element] motor is connected to a physical, rotational device operated at a slow speed.

9. (Once Amended) A thrombolytic device as in claim 1, wherein[:] said catheter wall has a braided construction.

10. (Once Amended) A thrombolytic device as in claim 1, wherein[:] said catheter wall has a plurality of flexible projections extending externally therefrom.

11. (Once Amended) A thrombolytic device as in claim 10, wherein[:] said flexible projections are selected from the group consisting of brushes, bristles, deformable mesh braid, flexible wires and tentacles.

12. (Once Amended) The thrombolytic device of claim 1, further comprising[:]
a motor controller connected to said motor, said motor controller is capable of controlling the speed of the motor from 0.1 to 600 revolutions per minute.

13. (Once Amended) A thrombolytic device as in claim 12, wherein[:] said motor controller is programmable by the user as to motor speed, activation time, and deactivation time.

14. (Once Amended) A thrombolytic device as in claim 13, wherein[:] said motor controller is programmable by the user to control a motor speed[,] of from about 0.1 and 600 revolutions per minute, an activation time, and a deactivation time.

16. (Twice Amended) A thrombolytic device for use with a pharmacological agent comprising:

a catheter having a catheter wall, a proximal end, a distal end, and at least one lumen;

a motor attached to said proximal end of said catheter for imparting motion to said catheter along a segment of said catheter between said distal end and proximal end, said motion being capable of disrupting a thrombus;

a pharmacological delivery conduit with a first end and a second end, said first end operatively connected to said lumen at said proximal end of said catheter;

a pump for delivering a pharmacological agent, said pump operatively connected to said second end of said conduit.

20. (Twice Amended) A pharmomechanical device, comprising:

means to increase the surface area of a clot in a vascular structure such that said clot can be dissolved by a lytic agent; and

means for providing mechanical motion to a catheter [action] throughout a length of a vessel for a prolonged period of time while said lytic agent is acting, said [mechanical] means for providing mechanical motion comprising a corkscrew catheter configuration substantially incapable of damaging an endothelium of said vascular structure, said means for providing mechanical motion causing said catheter to rotate once it is inserted inside a patient.

24. (Once Amended) The device as set forth in Claim 20, wherein said [the mechanical] means for providing mechanical motion operates intermittently and over a prolonged period of time.

25. (Once Amended) The device as set forth in Claim 24, wherein said [mechanical] means for providing mechanical motion [intermittent operation] provides for a time of inactivity at least as great as a time of activity of said device.

26. (Once Amended) The device as set forth in Claim 20, wherein said [mechanical] means for providing mechanical motion generates vibrations effective to disrupt a clot, but does not promote hemolysis or cause[s] damage to an endothelium.

27. (Once Amended) The device as set forth in Claim 20, wherein said device extends for a substantial length of said vessel[over which said mechanical action is conducted].

31. (Twice Amended) A method for ameliorating a clot in a patient's blood vessel, comprising:

administering to a patient an amount of contrast medium to determine the extent of a thrombus in the patient's blood vessel;

selecting a catheter having an appropriate length segment, said length segment having a mechanically active portion and an aperture-containing portion, said step of selecting conducted so that said length segment spans the entire length of a clot contained within said patient's blood vessel;

inserting a catheter into said patient's blood vessel;

deploying a distal occlusion element to reduce undesired passage of a thrombolytic drug from said blood vessel;

programming a motor controller to obtain desired periods of activation and inactivation of said mechanically active portion;

intermittently activating said mechanically active segment to remove said clot from said blood stream;

infusing a desired thrombolytic agent through said catheter when [substantially simultaneously with said step of activating] said mechanically active portion is activated [segment]; and

observing the patient in a location remote from the patient during at least one of said steps of intermittedly activating and infusing.

41. (Once Amended) The device as set forth in Claim 20, wherein an intermittent mechanical motion of the catheter is caused by the delivery of [provided by a pump that delivers] a lytic agent in [programmable] pulses, said pump being programmable to deliver the lytic agent in pulses.

42. (Once Amended) The device as set forth in Claim 41, wherein said pump is programmed to deliver said lytic agent at a desired [a] frequency or [and a] duration[of said pulses are programmable].

Marked-up

Mechanically Active Infusion Catheter

Related Application

This application claims priority from U.S. Provisional Patent Application No. 60/140,886 filed on June 24, 1999.

Field of the Invention

The present invention relates to a device and method utilized within the medical field to dissolve or eliminate blood clots that may block arteries, veins, grafts, implants, stents, catheters, and other structures. In one embodiment, pharmacological and mechanical action is combined to achieve this result.

Background of the Invention

The presence of thrombus, or blood clot, within arteries, veins, grafts, and vascular channels of the bodies is a challenge to many disciplines of medicine. If the thrombus develops acutely, it may create a medical emergency. Even if the thrombus develops gradually, conservative medical management with drugs is frequently less than satisfactory. Surgical intervention is an alternative, although a costly, and, at times, an ineffective one in many cases. Catheter directed thrombolysis is effective, but time consuming and very costly, because of the expense of the drug and the intensive care needed to monitor this therapy. A successful catheter infusion thrombolysis may take 36 to 48 hours to achieve complete thrombolysis.

Mechanical thrombolytic devices have been developed which are quick and effective in dialysis grafts, mainly because of the nature of such fresh unorganized clots presented in such situations, but such devices are not effective in removing most of the thrombus in arteries and veins of the body. Many of these mechanical devices have the potential to damage the endothelium of the arteries and veins, as well. The endothelium is a fragile covering of the inside of arteries and vessels, and is easily damaged with mechanical forces. This may cause a cascade of events resulting in thrombosis, restenosis, accelerated atherosclerosis, valvular dysfunction, platelet aggregation, late

thrombus formation, and other untoward events. By damaging the endothelium during percutaneous thrombolysis, long term patency of the vessel is compromised.

Many mechanical thrombolytic devices have been developed to hasten the process of non-surgically eliminating clot from blood vessels, but in most cases, they fail to remove all of the clot. This necessitates an additional procedure of protracted infusion of a thrombolytic drug, which is the procedure the mechanical thrombolytic devices were designed to replace.

Mechanical devices exist that also deliver a drug to aid in the dissolution of thrombus, but are utilized and then removed, usually in 20-40 minutes. Such methods and devices do provide mechanical action over a protracted period of time while the drug is being infused. As a result, there is invariably thrombus remaining at the termination of the procedure, necessitating the infusion of a thrombolytic drug through a different catheter for a protracted period of time to eliminate the remaining clot. This proves costly as more resources in the form of personnel and the expensive drugs are consumed.

The prior art mechanical thrombolytic devices and the prior art combination mechanical-pharmacologic devices are therefore designed to be operated mechanically for short periods of time, usually 20-40 minutes total, and at very high speeds or frequencies. Prior art devices are designed to act in short, intense bursts and involve rotating baskets and brushes, propellers, water jet, Venturi effect, vibrational, and other mechanical methods. The mechanical action is often effective in debulking, or lessening, the clot burden, but rarely effective in removing or dissolving all of the clot. Part of the reason is that a clot adherent to the wall of the vessel is not affected by these mechanical devices. The use of these devices to perform the incomplete mechanical thrombolysis necessitates a procedure which demands the attention and the time of a physician, a nurse, and several technologists in an interventional suite, catheterization lab, or operating room.

The prior art devices are also expensive, typically costing $500-700 or more. This tremendous expenditure of time, effort, and supplies is usually not rewarded with complete success, creating a need to place another expensive infusion catheter within the clot, transferring the patient to an intensive observation area, and infusing thrombolytic drug(s) for a protracted period. The patient is then returned to the interventional suite

many hours later, and most often, the action of the thrombolytic drug has resulted in complete thrombolysis with no residual clot.

The net consequence is that a lot of time, energy, personnel, and money are expended with the use of prior art mechanical and pharmaco-mechanical devices, with incomplete results, necessitating the use of a relatively long infusion to effect complete thrombolysis. Therefore, the use of the prior art devices to dissolve a clot during the course of a procedural intervention is unsatisfactory, and an unnecessary consumption of resources. Moreover, the design and speeds at which such devices operate risk significant injury to a patient.

The existing mechanical and pharmacomechanical devices also suffer from a design that limits the thrombolytic action to an area near the tip of the catheter. This is true of the rotating baskets, propeller type devices, rotating brushes, water jet, ultrasonic, sub-sonic, vortex, and other mechanical thrombolytic devices. Many of these can be activated for only short periods of time, i.e., seconds or minutes, lest they overheat or cause hemolysis or blood loss. There is a real potential for many of them to damage the endothelium, or lining of the blood vessels, if used for more than a few seconds at a time. Moreover, the pharmacomechanical devices have apertures for injecting the thrombolytic drug near the tip of the catheter as well. While these designs may be satisfactory for a short segment occlusion of 10 cm. or so, frequently the occlusion because of thrombus is much longer. Such prior art devices must be advanced and retracted within the lumen of the occluded vessel to "treat" one segment of the vessel at a time, usually resulting in incomplete and ineffective treatment of the entire occluded segment, thus requiring the need for the patient to undergo a prolonged infusion of the thrombolytic drug with the attendant increase in costs. Typically, the thrombus within the deep venous system of the leg needing interventional therapy extends from the calf veins to the inferior vena cava, a length of 40-60 cm. Femoral-popliteal arterial grafts are 30 cm. or so.

There are many prior art devices for the treatment of thrombus or blood clot within the arteries and veins of the body, as the occurrence of blood clots is a common and serious medical condition. The trend toward lesser invasive procedures has benefited patients in improved outcomes, less morbidity, and without the need for surgery. There

are many prior art catheters designed for infusion of lytic agents, such as urokinase and tissue plasminogen activator substance (tPA). Representative of these are U.S. Pat. Nos. 4968306, 5250034, 5267979, 5624396, 5782797, and 5425723. The process of infusion and dissolution of the thrombus is a lengthy one, taking 24 to 48 hours frequently. The lytic agent bathes the thrombus and pharmacologically dissolves the thrombus over time. Such methods necessitate the use of a large amount of expensive drug or lytic agent and overnight monitoring in a critical care unit. The process may cost upwards of $20-30,000.

Purely mechanical thrombolytic devices were developed as an alternative to infusion thrombolysis. These devices attempt to dissolve the clot in a relative short procedure, usually less than an hour. Representative of these are U.S. Pat. Nos. 4747406, 4923462, 5569275, 5397293, 5766191, and 5997558. While they may be effective in removing a large amount of the thrombus in a relatively short period of time, there is usually incomplete thrombus removal necessitating further infusion of lytic agents to dissolve the residual thrombus. Moreover, they remove enough of the clot so that partial flow may be reestablished within the vessel, causing the lytic agent to be washed out of the clot containing vessel as it is being infused.

Combination devices which utilize mechanical thrombus disruption and pharmacological agent infusion are represented by U.S. Pat. Nos. 5279546, 5197946, 5362309, 5279456, 5725494, and 5713848. These combination devices are an improvement, in that they attempt to utilize a lytic agent and mechanical motion of various types to disrupt the clot. They however, are time inefficient and the action of the lytic agent usually takes hours to achieve complete thrombolysis. All of the prior art combination devices are used within the confines of a procedural intervention that takes less than an hour and would damage the endothelium if used for more protracted periods of time. Many would overheat or fail, as the mechanical motion demands high frequency vibrations or rotation. Even Dubrul, U.S. Pat. No. 57313848 at the lowest frequency of one vibration/second, would damage the endothelium if activated for several hours.

There is a dichotomy in the design of all of these prior art thrombolytic catheters. The pure infusion catheters only passively bathe the clot and have no method of

increasing the surface area of the clot to be dissolved. They demand very protracted infusions to clear the clot. The purely mechanical devices diminish clot burden, at a cost of time, materials, and personnel, but frequently leave significant residual clot requiring a prolonged infusion. The combination pharmaco-mechanical devices attempt to fragment the clot and deliver the lytic agent simultaneously, but are only able to be mechanically active for short periods of time, usually not enough time for the lytic agent to dissolve the clot.

Therefore, there is a need for a device which provides a mechanical action to increase the surface area of the clot for efficacious dissolution by the lytic agent, provides this mechanical action for a prolonged period of time while the lytic agent is acting, provides a mechanical action which is not harmful to the endothelium of the vessel, and is time efficient for the operator and the patient.

Summary of the Invention

The device of the present invention differs from all of the prior art devices in that it provides a mechanical means of gradually disrupting the clot as the lytic agent is acting, usually over a few hours. It overcomes the problems of potential mechanical failure or endothelial damage which would occur should the other pharmaco-mechanical devices be used over a period of several hours. It overcomes the problem of trying to dissolve some of the clot with an expensive mechanical device and all of the attendant problems listed above. It overcomes the problem of extremely protracted passive infusion thrombolysis.

The device of the present invention obviates the need for the above described prior art procedural interventions and use of prior art devices by providing a device which is simply placed into the clot or thrombus, and the intermittent mechanical action and continuous or intermittent infusion of lytic agent occurs, preferably, after the patient has been transferred to the observation area. As more completely described below, the present invention saves the step of intense mechanical intervention, saving costs in time, personnel, and materials. The present invention also lessens the time and the amount of drug needed for thrombolysis when compared to standard non-mechanical infusion thrombolysis.

The present invention satisfies the long-felt, but unsolved need for a pharmacomechanical thrombolytic device that will be effective over lengths of vascular veins and arteries and which can be utilized continuously, or intermittently, over several hours to allow the thrombolytic drug to be completely dissolve the thrombus. The mechanical component of the present invention disrupts the clot and provides more surface area for the thrombolytic drug to act upon.

Accordingly, it is one object of the current invention to solve the problems experienced in using prior art devices and methods by providing a device that is mechanically active over a substantial length of the catheter while allowing the thrombolytic drug to be infused or injected over the same substantial length of the catheter. It is also an object of the present invention to permit synergy of the mechanical and pharmacologic actions over a prolonged period of time, i.e., up to several hours, without damaging the endothelium of the vessel containing the clot. It is an object of the current invention to combine two elements: 1) pharmacomechanical device having a working length sufficient to span most or all of the length of a clot, and 2) provision of means to allow the pharmacomechanical action to occur over a protracted time period. Another object is to create cost efficiencies by diminishing the time and amount of drug to realize thrombolysis.

Brief Description of the Drawings

Fig. 1 is a depiction of a prior art thrombolytic catheter.

Fig. 2 is a depiction of a prior art pharmacomechanical thromblytic device. The brushes 6 near the tip provide the mechanical disruptive action and one or two side holes 10 immediately proximal to the brushes 6 allow infusion of the thrombolytic drug.

Fig. 3 is a depiction of the distal tip of a prior art mechanical thrombolytic device showing a propeller blade 7 used to create a vortex which disrupts a clot.

Fig. 4 demonstrates the major arteries of the body, with the right superficial femoral artery 2 representing thrombus 1 prior to catheter directed thrombolysis.

Fig. 5 demonstrates the major veins of the body, with right iliofemoral venous 3 thrombosis prior to catheter directed thrombolysis illustrated.

Fig. 6 represents the catheter device 18 of the present invention entering the left common femoral artery 4 directed into and through the thrombosed artery 2 in figure 4, the mechanically active segment and the infusion segment 26 span the entire length of the clot 1.

Fig. 7 represents the catheter device 18 of the present invention entering the right popliteal vein and the pharmacomechanical active segment ~~spaning~~26 spanning the entire length of the clot 1.

Fig. 8 demonstrates a deformable mesh braid 45 of an occluding element 38 in an undeployed, longitudinal, tubular orientation, and showing the inner core 42 and the outer surface 43 of the wire 20.

Fig. 9 demonstrates the occluding element 38 comprising mesh braid 45 in a deployed radially expanded state. The element 38 occludes the lumen of the vessel and prevents the thrombolytic drug from being washed away from the area of the thrombus. It should be noted that the outer 43 or inner core 42 of the wire 20 may be of varying stiffness, i.e., stiff proximally and limber distally, to facilitate the mechanical action of the device 18. Also the occluding element 38 may be used as a tensioner to facilitate the mechanical action, and as a clot dragger to remove residual thrombus.

Fig. 10 is a representation of the device demonstrating, from left to right, the drive motor 14 with the controller 13 incorporated, a "Y" adapter 16 to receive the line from the drug infusion pump 12, the outer sheath 22 to prevent the proximal portion 24 of the catheter from being mechanically active, the mechanically active segment 26 of the device 18 containing infusion apertures 10, and the occluding element 38. The arrows indicate motion of the mechanically active segment 26. Preferably the mechanically active segment 26 of the device contains only one lumen 28 which will house the guide wire 20 of the occluding element 38 and allow the thrombolytic drug to be infused. The wall of the device may incorporate braided wires or other stiffening material to facilitate the mechanical action.

Fig. 11 illustrates the mechanically active segment 26 with the infusion apertures 10 present within the popliteal, femoral, and iliac veins 3 of a patient. The occluding element 38 is deployed.

Detailed Description of the Preferred Embodiment

The current invention may take any one of several forms, but the preferred embodiment is that of a catheter (hereinafter meant to generally refer to any guide wire, infusible wire, or similar conduit) which is capable of delivering a thrombolytic agent and creating mechanical disruption of the clot while the thrombolytic agent is being delivered. The mechanical motion or mechanical action can take one of several forms which are described below. The mechanical motion is intermittent and more gentle than prior art devices to prevent hemolysis and endothelial damage. The mechanical motion is slower (e.g., less than 200 rpm, more preferably less than about 600 rpm, and most preferably less than about 55 rpm) than prior art devices and the mechanical motion occurs intermittently, at preselected intervals. The mechanical action is therefore of a non-rapid type which can be adjusted for different slow speeds. As an example, the mechanical action may be activated for two seconds and then inactive for five minutes, activated for two seconds and then inactive for five minutes, and so on until thrombolysis occurs. Various factors influence the choice of the parameters of speed of action (rpm's or cycles/sec), time of activation, time of inactivation, total treatment time (time of activation plus time of inactivation), repetition time, as well as the infusion rate of the lytic agent. These factors include the location of the clot, as more aggressive thrombolysis with rapid speed of action, longer activation times and shorter inactivation times can be achieved within grafts as there is no concern of damaging the endothelium. However if the thrombus is within a native artery or vein, the speed would be slower, time of activation shorter, and time of inactivation longer to keep from damaging the endothelium. The age of the clot or thrombus is a critical determinant in the total treatment time, as fresh or subacute clot (hours to a few days) will dissolve more quickly and easier than a clot which has been present for longer than 10 days or so. The size of the clot also is a determinant in the choices. A less aggressive (shorter activation times) and shorter total treatment time is chosen for a relatively small clot of recent vintage. The parameters for the lytic therapy infusion may be varied as well depending on the site, age

of thrombus, size of thrombus, etc. Therefore, the preferred embodiment and preferred parameters may be site specific.

Generally, the device 18 of the present invention (Fig. 6) comprises an infusion pump 12 which infuses the lytic agent at a continuous selected rate. The device 18 of the present invention is simply placed into the clot 1 and the patient sent to an observation area where the lytic agent and mechanical action occur. The interventionalist, team, and suite are free to perform other cases while the intermittent mechanical action and lytic agent infusion are being achieved.

In one alternative embodiment, the lytic agent is infused intermittently (e.g., over a period of minutes, such as every 5-15 minutes, or even longer time periods, such as every ½ hour, etc.). The mechanical action may be selected from a range of 0.1-600 rpms with activation times of about 0.1 second to about 60 seconds, and inactivation times of 5 seconds to 20 minutes. Typically, the parameters chosen for a relatively fresh long segment lower extremity venous thrombus are: a) continuous infusion of the lytic agent, b) mechanical action speed of about 55 rpm's, c) activation time of at least about 3 seconds, and d) inactivation time of 3 minutes. Preferred parameters for a long segment arterial occlusion are: a) continuous infusion of the lytic agent, b) mechanical action speed of action speed of about 30 rpms (0.5 cycle/sec), c) activation time of at least about 2 seconds, and d) inactivation time of at least about 3 minutes. A preferred parameter setting for a graft is: a) continuous infusion of the lytic agent, b) mechanical action speed of about 300 rpms, c) activation time of about about 5 seconds, and d) inactivation time of about 1.5 minutes. Of course, as discussed above, the clinical setting and patient condition may require alternative parameters, and the above are suggested only as examples.

Intermittent action provides for relatively long periods of no mechanical action in which the endothelium is not contacted, scraped, or damaged. The slower action of 30-55 rpm's (less than 1 cycle/second) and the short activation times of 2-3 seconds prevents abrasion and damage of the endothelium as well. It is the intent of the current invention to provide a time of inactivity which is at least as great, and preferably substantially greater, than the time of activity of the device. This serves to protect the endothelium, but

also creates an environment for accelerated thrombolysis by the lytic agent. The slower speed of the mechanical action along with the very short activation times with relatively long periods of inactivation allows the mechanical action to continue for at least several hours while the lytic agent is acting to dissolve the clot. As an example, if the total treatment time is three hours, and a mechanical action speed of 30 rpm's is used with an activation time of 2 seconds, and inactivation time of 3 minutes, a total of only 60 cycles of mechanical action would occur in the entire treatment. This will be sufficient to create the environment for accelerated thrombolysis, but not sufficient to cause endothelial damage.

The endpoint is resolution of the clot, which will vary from patient to patient, location to location, and depend on the age and size of the clot amongst other factors. Typically, however, a total treatment time of about one to three hours is anticipated to lyse fresh venous and arterial thrombus with the above techniques, although total treatment times of about 30 minutes to about 36 hours are generally anticipated. The slower, intermittent mechanical action of the device augments the action of the lytic agent by enhancing admixture of the lytic agent and clot, by creating more surface area within the clot, and by mechanical disruption of the clot, while avoiding damage to the endothelium.

Alternative embodiments include a catheter (preferably a single catheter) with just a means to create the mechanical action, without any means to treat the thrombus pharmacologically. Another embodiment allows the infusion of the thrombolytic agent after the mechanical portion is activated. Both the mechanical and the pharmacological delivery elements 25,26 (Figs. 6, 7, 10, 11) preferably are effective over a substantial length of the catheter 18, rather than just concentrated at the tip, as is the case with prior art devices.

The mechanical element may be one of several types, i.e., ultrasonic, vibrational, rotational, bi-rotational, longitudinal motion, expansile, and the like. A suitable mechanical element may be a wire or a smooth wall catheter, have apertures 10 for the injection of the thrombolytic agent, or projections from the side of the device to better disrupt the ~~thrombus.~~thrombus (not shown.) A preferred embodiment uses wave like

undulations or vibrations to disrupt the clot slowly while the pharmacological agent is being infused. Since the mechanical motion is intended to be used for some protracted period of time, it is advantageous for the mechanical motion to be one which does not promote hemolysis nor damages the endothelium. A slower motion rather than a rapid motion is therefore desirable.

In one ~~embodiment, a motor~~embodiment (Fig. 10), a motor 14 that causes the catheter 18 to vibrate or undulate is attached to a wire 20 that is inserted within a lumen 28 of the catheter 18 or to the catheter 18 itself. Braiding within the wall of the catheter 18 to enhance transmissions of the vibrations may be utilized, and this may obviate the need to insert a wire 20 within the catheter 18. A stiff segment 24 of the catheter 18 proximally is desirable, as the efficiency of transmitting the vibrations from the motor 14 to the mechanical element segment 26 is then enhanced. One may compare this stiffer or more rigid proximal segment 24 to a fly rod transferring energy to a fly line or the handle of a bullwhip causing the action of the whip. Again, it is the intent that a substantial length of the intravascular portion of the catheter is provided with the mechanical action.

A separate sheath component (22, Fig. 10) through which the device 18 is inserted may be used to keep the entirety of the device 18 from being mechanically active. In this case, the outer sheath 22 houses a proximal portion 24 of the device 18 and the mechanically active portion 26 of the device 18 extends distal to the tip of the outer sheath 22. In one embodiment, the catheter 18, at least in the mechanically active segment 26, contains only one lumen 28, although more than one lumen is feasible.

Another method to accomplish an effective mechanical motion (not shown) is to place two wires in a catheter wall so that they are disposed on opposite sides of the lumen. The wires are moveable within the catheter wall proximally and affixed at a point at which the mechanical motion is to begin. An alternating to and fro motion of the two wires causes the catheter to undulate distal to the fixation point. A motor 14 provides the desired motion of the two wires.

Still another method of effective mechanical motion involves a catheter having a spiral shape in the distal desired length. Such a catheter is straight proximally 24, but of a spiral configuration in the desired mechanical element segment 26. A motor 14 causes

the catheter 18 to spin at a rather slow rate (approximately one to 300 times per minute). The proximal portion 24, because it is straight, does not have any substantial mechanical disruptive motion. The distal portion 26, because of the spiral configuration, spins in a corkscrew manner against the clot 1 or wall of the vessel, disrupting the clot.

Where the catheter includes a guide wire 20 to stiffen it, and where a lytic agent may be infused through side holes 10, the guide wire 20 may by spiral shaped as well. A guide wire (not shown) with a removable inner straight mandrel and an outer cylinder of shaped memory alloy may be utilized to create the spiral or corkscrew configuration. When the inner mandrel is within the outer sleeve or cylinder of the guide wire, the guide wire is stiff and more or less straight. When the inner core is removed the guide wire assumes a spiral configuration causing the infusion catheter over it to also assume a spiral or corkscrew configuration.

A variation of the above entails rotating the spiral catheter 18 one way and then the other, similar to an agitator in a washing machine. A motor 14 is provided to effect such motion. Yet another modification involves a serpentine or other shape to the catheter. Any motion can be employed with any different shape. Complex motions, such as a longitudinal wave like motion of the catheter combined with axial rotation, may be advantageous.

In another embodiment, an intermittent motion of the catheter is provided by a pump (not shown) that delivers lytic agent forcefully in programmable pulses. Such a pump is commercially available (AngioDynamics, Queensbury, N.Y.). It generates abrupt pulse waves which cause the lytic agent to be sprayed into the thrombus through side holes 10 in the catheter 18. Generally, the connecting tubes dissipate the motion caused when this abrupt and forceful pulse of medicine occurs. By more rigidly connecting the Pulse-Spray pump to the device of the current invention and preventing the dissipation of the pulse wave forces in the connecting tube, the pulse wave forces are transferred to the device of the current invention, causing it to move within the body. The connecting elements may be made of steel or any other rigid substance that is capable of transferring the forces from the Pulse-Spray machine to the catheter efficiently so that the catheter is mechanically active as described above. Since the frequency and duration of

pulses are programmable on the pump, a separate motor to move the catheter will not be needed. Alternatively, a flexible catheter may be provided which is serpentine or spiral in shape. The pulse of the Pulse-Spray pump will straighten the catheter from its original shape, causing desired motion within the clot while the lytic agent is being dispersed.

An intermittent motion may be provided to any of the embodiments, i.e., so that the mechanical motion is activated every few seconds, every few minutes, or for any given time period. In fact, this is desirable to prevent damage to the vessel endothelium, but allows for enough clot disruption to enhance the action of the thrombolytic agent. The present invention is intended to provide a slow, intermittent motion over several hours to allow a lytic agent to work completely while not damaging the endothelium. Of course, the device may employ mechanical motion without the addition of a thrombolytic drug. Therefore, the current invention differs from prior art devices in many respects, including shape, length of mechanically active segment 26, the rapidity of the motion, the programmability of the motor drive 14, shorter periods of activity, longer periods of inactivity, the ratio of periods of inactivity to periods of activity, the number of total cycles of mechanical action during a treatment, as well as other features described herein.

In one embodiment (Fig. 10), a catheter 18 is constructed with multiple apertures (side holes, slits, or other openings) 10 through which a thrombolytic drug, when utilized, is injected or delivered. A separate pump 12 controls the rate and duration of drug administration. The apertures 10 are positioned throughout the mechanical motion segment 26 of the catheter, which may include much of the body of the catheter in addition to the area near the catheter tip. The apertures 10 preferably occupy about 20-60 cm. of the distal aspect of the catheter, rather than the typical distal 10 cm. of other prior art devices, although the apertures may occupy from 5-60 cm. of the distal aspect of the catheter.

The motor 14 which drives the mechanical portion 26 of the device 18 are typically different than those of the prior art, which are designed to be utilized for a short time during a procedure and are typically hand held devices with a finger activation, which rotate at very high rpm's. The motor 14 of the current invention may be programmable 15 to rotate at slower rates (about 0.1-600 rpms) over much longer periods

of time (30 minutes-days.) In a preferred embodiment, the motor 14 may be programmed 15 to rotate, or have other mechanical action, at a mechanical action rate, or speed, of about 0.5 to 55 rpms and a total treatment time of about 30 minutes to 5 hours. The activation times may vary from about 0.1-60 seconds and the inactivation times may vary from about 5 sec to 20 minutes in the preferred embodiment. The program 15 may contain an intermittent mode in which there would be no motion provided by the catheter for specified periods of time. A motor~~controller, which is programmable,~~controller 13, which is programmable 15, may be incorporated into the motor 14 or may be separate. The motor housing 14a is designed to accompany the patient to the ward or critical care unit so that it can be monitored while the pharmacomechanical thrombolysis proceeds. A battery and/or electrical connections are ~~provided.~~ provided (not shown.)

Another aspect of the present invention (Figs. 8, 9, 10, 11), relates to an element 38 which occludes a vessel distal to the catheter 18 or, at least, distal to the mechanical and pharmacologic segments 26 of the catheter 18. This occluding element 38 can take any one of several forms, including an inflatable balloon (not ~~balloon,~~shown), a deformable mesh braid 45 with a membrane 41, a malecot with a membrane (not shown), or other suitable configuration. A preferred embodiment (Figs. 8, 9) consists of a deformable mesh braid 45 mounted on the outer surface 43 of a movable core guide wire 20. When the inner core 42 is retracted 44 in relation to the outer surface 43 (Fig. 9), the braid 45 changes from a longitudinal tubular structure (Fig. 8) to a radially expanded disc like structure (Fig. 9) which occludes the lumen of the vessel. The membrane 41 covers or is disposed in the interstices ~~of the braid. The wire~~46 of the braid 45. The wire 20 is preferentially inserted through the catheter 18 and may or may not be designed so as to assist in the motions of the catheter 18 described above. A primary purpose of this element 38 is to keep the pharmacologically active thrombolytic drug from washing out of the area of the clot 1 once some of the clot 1 has been dissolved. The prior art infusion catheters frequently are effective in restoring a channel within the clot, but subsequently the thrombolytic drug is washed away from the clot secondary to the success of~~re-~~ re-establishing flow. Further thrombolysis is the result of a systemic effect of the drug,

rather than the desired local drug delivery of the infusion catheter. This situation necessitates longer infusion times utilizing more expensive thrombolytic drugs. This translates into added costs to achieve complete thrombolysis. The occluding element 38 of the current invention would prevent the washout of the thrombolytic drug from the thrombus, accelerating the thrombolytic process. Protection against embolization is a secondary purpose.

Balloons have been used for greater than 30 years to temporarily occlude vessels. Filters are included in more recent prior art to protect against distal embolization, but the occluding device of the current invention, in the form of a malecot or deformable mesh braid 45 containing a more or less impermeable elastomeric membrane 41, has not been utilized before.

Therefore, the foregoing description details a unique device and method that creates time and cost efficiencies in removing thrombus from the vascular channels of the human body. The device differs from prior art in addition to those previously listed features, in: 1) the length of the mechanically active segment 26, 2) the distribution of the apertures 10 for drug insertion when combined with a mechanically active segment 26, 3) the configuration and programmability 15 of the motor drive 14, 4) the presence of a motor controller 13, 5) the distal occluding element 38, 6) need to move the mechanically active segment 26 within the clot (prior art), and 7) the inclusion of a combination of these features within one device. The device and method of the current invention also differs from prior art in that it expedites long segment thrombolysis, something that has never been achieved with prior art devices. The present invention provides for a short interventional procedure to place the device, begin infusion and initiate desired mechanical action. When the patient returns in one to several hours, the thrombolytic process is complete, the device can then be removed, and patient discharged shortly thereafter.

The present invention is preferably used to clear long segment occlusions secondary to thrombus within arteries, veins, and grafts. In the case of iliofemoral deep venous thrombosis (clot involving the iliac, superficial femoral, and popliteal veins), a preferred procedure is to percutaneously enter the popliteal vein via a Seldinger approach,

insert a multipurpose angiographic catheter, and inject a small amount of contrast medium centrally. This will determine the extent of the thrombus in the iliac vein. The initial catheter is then exchanged for the device of the current invention that is positioned so that the mechanically active segment 26, and the aperture containing segment 25, span the entire length of the clot. The lengths of these segments are chosen from one of several different models of the device so that the length of the active segments 26 matches the length of clot 1 within the patient. If desired the distal occlusion element 38 may be deployed at this time, or even before the catheter device 18 of the invention is inserted. The mechanical portion 26 of the catheter 18 is connected to the drive motor 14, and the infusion lumen 28 is connected to the drug infusion pump 12. Appropriate desired frequencies, actions, motions, pauses, etc., are programmed 15 into the drive motor controller ~~controller,~~13, and the motor 14 initiated. The flow rate of the thrombolytic drug is selected and the drug infusion pump 12 is begun. The patient is then transferred to a holding area, hospital room, or critical care unit for observation. The thrombolysis may be monitored by duplex compression ultrasound, but eventually the patient will return to the interventional suite to be evaluated with contrast injection, usually within three to five hours.

In the case of superficial femoral artery thrombosis or femoropopliteal bypass graft occlusion from thrombus, either the ipsilateral femoral artery or contralateral femoral artery may be entered by Seldinger technique. A contrast agent is injected to determine the extent of the clot, and the appropriate device 18 of the invention is chosen to match the length of clot within the patient. It is positioned, with or without the distal occlusion device 38, so that the mechanically active 26 and pharmacologically active 25 segments essentially span the entire clot 1. The connections are made as above, and the appropriate parameters chosen and programmed 15. The mechanical segment 26 and the pharmacological segment 26 are initiated. The patient is then handled as in the prior paragraph. An endpoint is reached when pulses are detected clinically, or when the patient is returned to the angiography suite to be restudied. Any residual debris within the vessel may be aspirated before removing the distal occlusion device 38.

In addition to the description and guidance provided herein, the present inventor provides additional written description and enablement support for the present invention by incorporation by reference of U.S. Patent Nos. 5,279,546 and 5,569,275.

It is obvious that variations of these methods may be employed to achieve the same desired effect. It is understood that various modifications of the device of the current invention and method may be accomplished within the scope of this invention.

What is Claimed is:

1. A thrombolytic device comprising:

a catheter having a catheter wall, a proximal end, a distal end, and at least one lumen;

a mechanical element, having a near end and a far end, said near end connected to said distal end of said catheter and extending therefrom; and

a motor attached to said proximal end of said catheter for imparting motion to said mechanical element.

2. A thrombolytic device as in claim 1, wherein:

said mechanical element is chosen from the group consisting of a vibrational device, a rotational device, a bi-rotational device, and expansile device, a wave-like undulating device, and a longitudinally-actuated device.

3. A thrombolytic device as in claim 1, wherein said mechanical element is a physical, rotational device operated at a slow speed.

4. A thrombolytic device as in claim 3, wherein said slow speed is less than about 600 revolutions per minute.

5. A thrombolytic device as in claim 3, wherein said slow speed is less than about 250 revolutions per minute.

6. A thrombolytic device as in claim 3, wherein said slow speed is less than about 100 revolutions per minute.

7. A thrombolytic device as in claim 3, wherein said slow speed is less than about 55 revolutions per minute.

8. The thrombolytic device of claim 1, wherein said catheter is a single catheter with a single lumen.

9. A thrombolytic device as in claim 1, wherein:

said catheter wall has a braided construction.

10. A thrombolytic device as in claim 1, wherein:

said catheter wall has a plurality of flexible projections extending externally therefrom.

11. A thrombolytic device as in claim 10, wherein:

said flexible projections are selected from the group consisting of brushes, bristles, deformable mesh braid, flexible wires and tentacles.

12. The thrombolytic device of claim 1, further comprising:

a motor controller connected to said motor, said motor controller is capable of controlling the speed of the motor from 0.1 to 600 revolutions per minute.

13. A thrombolytic device as in claim 12, wherein:

said motor controller is programmable by the user as to motor speed, activation time, and deactivation time.

14. A thrombolytic device as in claim 13, wherein:

said motor controller is programmable by the user to control a motor speed, of from about 0.1 and 600 revolutions per minute, an activation time, and a deactivation time.

15. A thrombolytic device as in claim 1, further comprising:

a sheath encompassing all but said far end of said mechanical element.

16. A thrombolytic device for use with a pharmacological agent comprising:

a catheter having a catheter wall, a proximal end, a distal end, and at least one lumen;

a mechanical element extending from said distal end of said catheter;

a motor attached to said proximal end of said catheter for imparting motion to said mechanical element;

a pharmacological delivery conduit with a first end and a second end, said first end operatively connected to said lumen at said proximal end of said catheter;

a pump for delivering a pharmacological agent, said pump operatively connected to said second end of said conduit.

17. The thrombolytic device of claim 16, further comprising:

a motor controller connected to said motor, and wherein said pump has a variable and adjustable delivery rate.

18. The thrombolytic device of claim 16, further comprising:

an occluding element with a first end and a second end, said first end connected to said far end of said mechanical element and extending therefrom, said second end having a occlusion mechanism for reducing dispersion of said pharmacological agent in an area where a clot resides.

19. A thrombolytic device as in claim 18, wherein said occlusion mechanism is selected from the group consisting of a inflatable balloon, a deformable mesh braid with a membrane, and a malecot with a membrane.

20. A pharmomechanical device, comprising:

means to increase the surface area of a clot in a vascular structure such that said clot can be dissolved by a lytic agent;

means for providing mechanical action for a prolonged period of time while said lytic agent is acting, said mechanical means substantially incapable of damaging an endothelium of said vascular structure.

21. The device as set forth in claim 20, wherein said period is at least about 5 hours.

22. The device as set forth in claim 20, wherein said period is at least about 10 hours.

23. The device as set forth in claim 20, wherein said period is at least about 24 hours.

24. The device as set forth in Claim 20, wherein the mechanical means operates intermittently and over a prolonged period of time.

25. The device as set forth in Claim 24, wherein said mechanical means intermittent operation provides for a time of inactivity at least as great as a time of activity of said device.

26. The device as set forth in Claim 20, wherein said mechanical means generates vibrations effective to disrupt a clot, but does not promote hemolysis or causes damage to an endothelium.

27. The device as set forth in Claim 20, wherein said device extends for a substantial length over which said mechanical action is conducted.

28. The device as set forth in Claim 20, further comprising an occluding element positioned so as to maintain desired concentration of a thrombolytic drug in a desired segment of a patient's blood vessels.

29. The device as set forth in Claim 24, wherein the ratio of an inactivation time to an activation time is greater than 1.

30. The device as set forth in Claim 24, wherein the ratio of an inactivation time to an activation time is greater than 50.

31. A method for ameliorating a clot in a patient's blood vessel, comprising:

administering to a patient an amount of contrast medium to determine the extent of a thrombus in the patient's blood vessel;

selecting a catheter having an appropriate length segment, said length segment having a mechanically active portion and an aperture-containing portion, said step of selecting conducted so that said length segment spans the entire length of a clot contained within said patient's blood vessel;

inserting a catheter into said patient's blood vessel;

deploying a distal occlusion element to reduce undesired passage of a thrombolytic drug from said blood vessel;

intermittently activating said mechanically active segment to remove said clot from said blood stream; and

infusing a desired thrombolytic agent through said catheter substantially simultaneously with said step of activating said mechanical segment.

ABSTRACT

A device and method to dissolve or eliminate blood clots from a patient relies upon a non-rapid moving mechanism to physically dissolve clots without damaging endothelium of the arteries and veins of a patient. In one embodiment, in addition to mechanical agitation of a clot, a thrombolytic agent is administered simultaneously with such agitation. Preferably, intermittent agitation is utilized over a prolonged period of time to effectuate clot removal.